L20 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

AB Previously reported studies from these labs. described the design of a novel series of high-affinity NK1 antagonists based on the 4,4-disubstituted piperidine ring system. Further structure-activity studies have now established that for high NK1 affinity the benzyl ether side chain must be 3,5-disubstituted and highly lipophilic, the optimal side chain being the 3,5-bis(trifluoromethyl)benzyl ether, 12 (hNK1 IC50 = 0.95 nM). Addnl. studies have shown that this class of NK1 antagonist tolerates a wider range of substituents on the piperidine nitrogen, including acyl (hNK1 IC50 = 5.3 nM) and sulfonyl (hNK1 IC50 = 5.7 nM) derivs. Following preliminary pharmacokinetic anal., two compds. were selected for in vivo study in the resiniferotoxin-induced vascular leakage model, both showing excellent profiles (ID50 = 0.22 and 0.28 mg/kg, resp.).

AN 1998:642712 CAPLUS

DN 130:32676

TI 4,4-Disubstituted Piperidine High-Affinity NK1 Antagonists: Structure-Activity Relationships and in Vivo Activity

AU Stevenson, Graeme I.; Huscroft, Ian; MacLeod, Angus M.; Swain, Christopher J.; Cascieri, Margaret A.; Chicchi, Gary G.; Graham, Michael I.; Harrison, Timothy; Kelleher, Fintan J.; Kurtz, Marc; Ladduwahetty, Tamara; Merchant, Kevin J.; Metzger, Joseph M.; MacIntyre, D. E.; Sadowski, Sharon; Sohal, Balbinder; Owens, Andrew P.

CS Department of Medicinal Chemistry Neuroscience Research Centre, Merck Sharp and Dohme Research Laboratories, Harlow Essex, CM20 2QR, UK

SO Journal of Medicinal Chemistry (**1998**), 41(23), 4623-4635
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

IT **160377-06-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(structure-activity relationships and in vivo activity of 4,4-disubstituted piperidine high-affinity antagonists)

RN 160377-06-0 CAPLUS

CN Piperidine, 4-[[[3,5-bis(trifluoromethyl)phenyl]methoxy]methyl]-4-phenyl-1-(2-phenylethyl)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 160376-11-4
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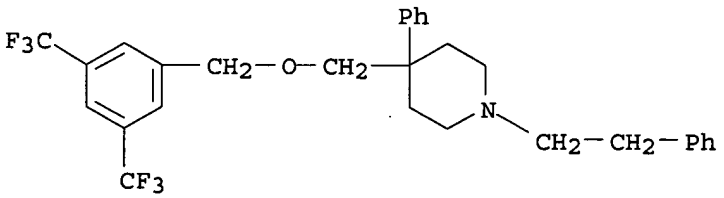

CM 2

CRN 104-15-4
CMF C7 H8 O3 S